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AUG 30 2006

Atty Dkt. No.: 10010632-3  
USSN: 10/611,409

**REMARKS**

In view of the following remarks, the Examiner is requested to allow Claims 21-34, as well as new Claims 42 to 43, the only claims pending and under examination in this application.

Claim 21 has been amended to indicate that the cleavage of the 3' cleavable tag from the at least one complementary nucleotide extension product produces both a cleaved tag, which is not bound to a nucleotide, and an extension product that includes the at least one complementary nucleotide that is still hybridized to the nucleic acid sequence. Support for this amendment can be found throughout the specification and claims as originally filed. In particular, support may be found at page 9, line 22 to page 10, line 9. Claim 22 has been amended to define cdNTP. Support for this amendment can be found at page 4, line 20 to page 5, line 5. New Claim 42 finds support in the originally filed claims, as well as in the specification at page 6, lines 13-15. New Claim 43 finds support in the originally filed claims, as well as in the specification at page 14, lines 7-11. Accordingly, no new matter has been added.

As no new matter has been added by way of these amendments, entry thereof by the Examiner is respectfully requested.

***Double Patenting***

Claims 21-34 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of US Patent No. 6,613,523.

Accordingly, filed herewith is the requisite terminal disclaimer in view of which the Applicant respectfully requests these rejections be withdrawn.

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***Claim Rejections – 35 U.S.C § 112, second paragraph***

Claims 21-34 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 22 and 23 have been rejected as allegedly vague and indefinite because the phrase "cdNTP" is allegedly unclear. Accordingly, Claim 22 has been amended to indicate that the term "cdNTP" means a cleavable tag terminated deoxynucleotide triphosphate. The Applicant contends that in light of the amendments made herein this rejection has been rendered moot and respectfully requests that it be withdrawn.

Claim 27 has been rejected as allegedly vague and indefinite because it is allegedly unclear how the extension product is produced by a ligase in the presence of the oligonucleotide. The Applicants respectfully disagree and contend that the specification clearly teaches that a complementary oligonucleotide that is 3' end labeled with a cleavable tag may be hybridized to a DNA template and that the hybridized complementary oligonucleotide may then be ligated by a ligase to a primer on the DNA template so as to produce an extension product. See page 12, line 17 to line 23 and page 32, lines 14 to 23. Accordingly, in view of the teachings of the specification, one of skill in the art would understand that the extension product is produced by the ligase ligating the oligonucleotide to the primer. Hence, the Applicant contends that Claim 27 is definite and clear as written and respectfully requests that this rejection be withdrawn.

Claims 25-27 has been rejected as allegedly vague and indefinite because it is allegedly unclear how "an oligonucleotide" is used in the extension of the primer nucleic acid.

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The Applicants respectfully disagree and contend that the specification clearly teaches that a complementary oligonucleotide that is 3' end labeled with a cleavable tag may be hybridized to a DNA template and that the hybridized complementary oligonucleotide may then be ligated by a ligase to a primer on the DNA template so as to produce an extension product. See page 12, line 17 to line 23 and page 32, lines 14 to 23. Accordingly, in view of the teachings of the specification, one of skill in the art would understand that the primer nucleic acid is extended by being ligated to the oligonucleotide. Hence, the Applicant contends that Claims 25-27 are definite and clear as written and respectfully requests that this rejection be withdrawn.

Claims 21-34 has been rejected as allegedly vague and indefinite because although the preamble recites a method of determining a nucleic acid sequence, the claims do not have an active step reciting how the nucleic acid sequence is determined. Claim 21 has been amended. The Applicant contends that this rejection has been rendered moot in view of the amendments to Claim 21. The Applicant, therefore, respectfully request that this rejection be withdrawn.

### ***Claim Rejections – 35 U.S.C § 102***

Claims 21-31 and 33-34 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Schmidt et al. (WO 99/02728).

According to the M.P.E.P., a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the claim. See MPEP § 2131.

Claim 21 is directed to a method of determining a nucleic acid sequence. The method, as amended, includes the steps of hybridizing a primer nucleic acid to a template nucleic acid, extending the primer by one complementary nucleotide that includes a 3' cleavable tag, and cleaving a 3' cleavable tag from the extension product to produce a cleaved tag, which is not bound to a nucleotide, and an

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extension product that includes at least one complementary nucleotide that is hybridized to the nucleic acid sequence. Accordingly, an element of Claim 21 is the cleaving of a 3' cleavable tag from the extension product to produce a cleaved tag and an extension product that includes at least one complementary nucleotide that is hybridized to the nucleic acid sequence.

Nowhere does Schmidt teach cleaving a 3' cleavable tag from the extension product to produce a cleaved tag and an extension product that includes at least one complementary nucleotide that is hybridized to the nucleic acid sequence. Schmidt does not teach this because Schmidt teaches that the extension product is to be dissociated and separated from the nucleic acid template prior to cleaving the cleavable tag from the nucleic acid. See page 45, first full paragraph:

are shown in Figure 15. Prior to cleavage of labels one needs to separate the Sanger ladder into its component fragment lengths. In a mass spectrometry system this stage can be coupled to the sample loading in a LCMS system. Separation into bands can be achieved by capillary zone electrophoresis. This will then pass through a UV spectrometer to determine the quantity of DNA in each band. Following this the sample will then pass through a photocleavage module to release the mass-labels which will then be injected into an electrospray mass spectrometer for analysis of the labels in each band.

As can be seen above, the method disclosed by Schmidt requires that the extension product fragments be dissociated from the DNA template and separated into a ladder based on their respective weights (e.g., via capillary electrophoresis). Once the fragments are separated by weight into individual bands the mass label is cleaved and passed into the spectrometer for analysis.

Accordingly, because Schmidt discloses that the extension product is to be separated from the nucleic acid template prior to cleaving the cleavable tag from the nucleic acid, Schmidt does not teach the cleaving of a 3' cleavable tag from the extension product to produce a cleaved tag and an extension product that includes at least one complementary nucleotide that is hybridized to the nucleic acid

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sequence. Therefore, Schmidt does not anticipate the claims as amended, because it fails to teach every element of the rejected claims. Hence, the Applicant respectfully request that the 35 U.S.C. § 102(b) rejection of Claims 21-31 and 33-34 be withdrawn.

New Claims 41 and 42 are also patentable distinguished from the cited art by virtue of elements present in these claims.

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### CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Timothy Joyce at 408-553-2510.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1078, order number 10010632-3.

Respectfully submitted,  
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Enclosure(s): Terminal Disclaimer as to US Patent No. 6,613,523

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